EXHIBIT

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Asbestos-Related Radiographic Changes by ILO Classification of 10 × 10 cm Chest X-Rays in a Screening of the General Population

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A sample of 1388 10 × 10 cm chest X-rays from a previous population screening of males aged 40+ years were reevaluated by use of the ILO classification. There were 1036 films of subjects from an industrialized town, and 352 from a rural community. The observed rates of parenchymal changes (profusion ≥ 1/0) at the reevaluation were 1.3% in the urban community and 3.4% in the rural community. The corresponding figures for pleural changes were 5.0% and 0.6%, respectively. Based on additional questionnaire information on asbestos exposure, it was found that the radiographic changes were probably related to past asbestos exposure for 2.3% of the subjects from the urban community and 0.6% from the rural community. In cases of asbestos-related illnesses the mean time since first exposure to asbestos was 35.9 years, whereas the mean duration of the exposures was 11.4 years. The results seem to indicate that the ILO reassessment of the radiographs was more sensitive in detecting pleural changes than the previous clinical screening of both small and large films.

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1076-2752/95/3702-0189$3.00/0

In a previous screening investigation of 21,453 males aged 40+ years in the county of Telemark, Norway, it was found that 18.1% had been exposed to asbestos at work.[1] The prevalence rate of pulmonary asbestosis was 0.4%, and that of asbestos-related pleural plaques was 1.8%.[2] These results were obtained by a primary screening with 10 × 10 cm chest X-rays combined with a clinical reexamination, including full-size chest X-rays of subjects with suspected findings. Previous asbestos exposure was determined by a questionnaire in the primary screening and by interview of those who attended the clinical examination.

Previous studies have shown substantial variation in the prevalence rates of asbestos-related illnesses as determined by different diagnostic procedures.[3,4] In a North American reevaluation by use of the ILO classification, only 16 (3.6%) of 439 radiographs of subjects previously designated as having an asbestos-related disorder were found to have radiographic signs consistent with such a disorder.[5]

In the present study a sample of the 10 × 10 cm chest X-rays from our earlier study were reexamined by use of the ILO classification[6] to reevaluate the previously assessed prevalence of asbestos-related illnesses in the study population.

Subjects and Methods

From the previously screened populations of the industrial town

TABLE 1
Prevalence (%) of Radiographic Findings by ILO Classification of 10 × 10 cm Chest X-Rays from an Urban and a Rural Community

	Small opacities prof. ≥ 1/0	Small opacities prof. ≥ 1/1	Pleural thickening chest wall	Pleural thickening diaphragm	Pleural calcification	Diffuse pleural thickening	Any pleural changes
Urban (n = 1036)	1.3 (13)	0.7 (7)	3.6* (37)	3.1** (32)	3.1** (32)	0.3 (3)	5.0** (52)
Rural (n = 352)	3.4* (12)	1.4 (5)	0.3 (1)	—	0.3 (1)	0.3 (1)	0.6 (2)
All (n = 1388)	1.8 (25)	0.9 (12)	2.7 (38)	2.3 (32)	2.4 (33)	0.3 (4)	3.9 (54)

Numbers of subjects are in parentheses.
* $P < 0.05$.
** $P < 0.01$.

TABLE 2
Prevalence (%) of Asbestos-Related Illnesses in an Urban and a Rural Community Based on ILO Classification of 10 × 10 cm Chest X-Rays and Questionnaire Exposure Information

Community	Lung fibrosis ± pleural changes	Circumscribed pleural thickening	Diffuse pleural thickening	Pleural calcification	Total with asbestos-related findings
Urban (n = 1036)	0.3 (3)	1.8 (19)	0.1 (1)	1.6 (17)	2.3 (24)
Rural (n = 352)	0.6 (2)	0	0	0	0.6 (2)
All (n = 1388)	0.4 (5)	1.4 (19)	0.1 (1)	1.2 (17)	1.9 (26)

Numbers of subjects are in parentheses.

Porsgrunn and the rural municipality Seljord two rolls of film were selected by chance for reevaluation. In the following the two communities are referred to respectively as "urban" and "rural." All 10 × 10 cm X-rays had been taken in posteroanterior and lateral projections. The films were classified by the reassessment by one experienced reader (GH) according to the ILO system. All films were analyzed through a magnifier that yielded a 25% enlargement. During the classification of the films the reader had no information about the origin of the films, previous asbestos exposure, or the domiciles of the study subjects.

The study subjects were considered to have been exposed to asbestos whenever they had confirmed work-related asbestos exposure in the questionnaire from the primary screening. In the previous study the specificity of true positive answers, assessed by interview by a trained occupational physician, was 97.3%. The sensitivity of the questionnaire in identifying exposed subjects was 44.6%.[2]

Whenever the present ILO classification unveiled typical radiographic changes, and previous asbestos exposure was confirmed in the questionnaire, the findings were considered to be probably asbestos related.

Statistical analysis of differences between means was based on the standard errors of the differences. Analysis of differences between rates was based on the χ^2 test with Yates correction for small numbers.

Results

There were 1036 10 × 10 cm X-rays eligible from the urban community and 352 from the rural. The mean ages of study subjects from the rural and urban communities were 62.8 (SD 11.8) and 59.4 (SD 11.1) years, respectively ($P < 0.001$). There were significantly ($P < 0.01$) more smokers in the urban population, with 38% current smokers, 33% ex-smokers, and 29% never-smokers compared to 22%, 27%, and 51%, respectively, in the rural population.

Table 1 presents the prevalence rates of radiographic findings as determined by the ILO classification. In all, 75 (5.4%) had any findings described. Small opacities with profusion ≥ 1/0 were seen in 13 (1.3%) from the urban community and in 12

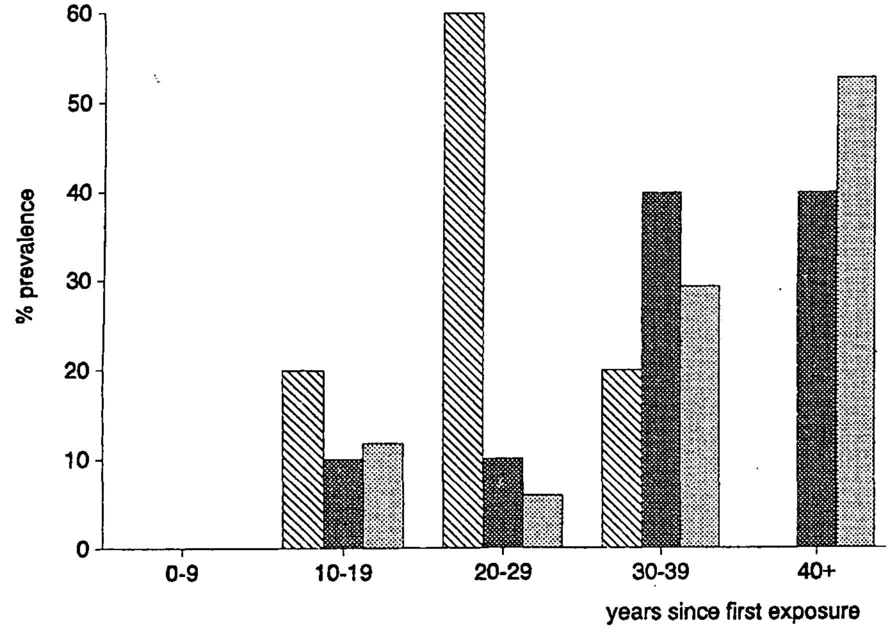

Fig. 1. Time since first exposure in 5 subjects with lung fibrosis with profusion 1/0 +, 20 subjects with pleural thickening, and 17 subjects with pleural calcification.

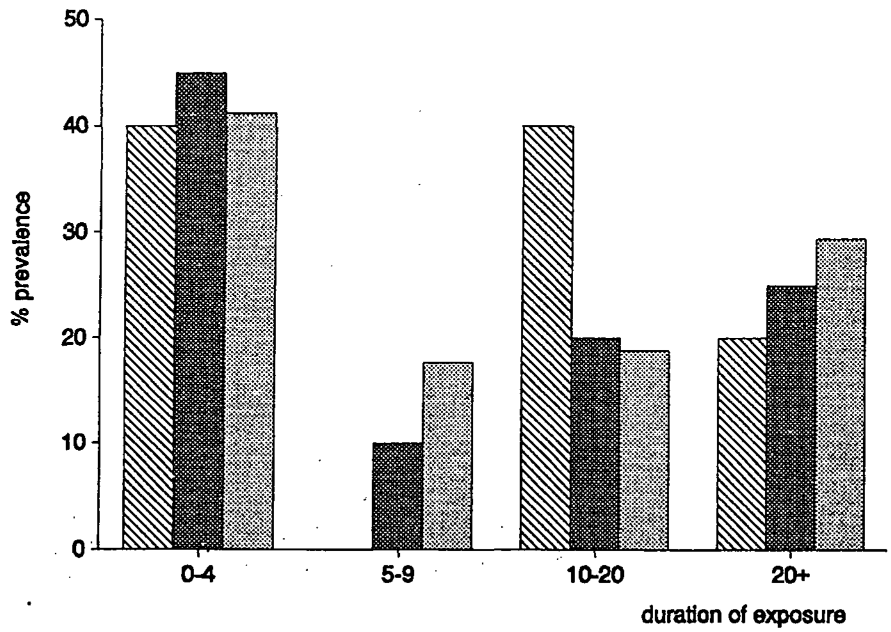

Fig. 2. Duration of asbestos exposure among 5 subjects with lung fibrosis with profusion 1/0 +, 20 subjects with pleural thickening, and 17 subjects with pleural calcification.

(3.4%) from the rural community ($P < 0.05$). For any pleural changes the corresponding figures were 52 (5.0%) and 2 (0.6%) ($P < 0.01$).

Previous occupational exposures to asbestos had been confirmed in the questionnaire by 22.1% of the urban participants and by 5.7% of the rural.[1] Table 2 presents the prevalence rates of illnesses that are probably asbestos-related in the two populations, based on the ILO classification and the questionnaire information. The rates of all asbestos-related findings was 2.3% among subjects in the urban community and 0.6% in the rural community ($P < 0.1$).

Figs. 1 and 2 present the time since first exposure and the duration of the reported exposures for subjects with asbestos-related lung fibrosis (profusion $\geq$ 1/0), pleural thickening, or pleural calcification. The mean times since first exposure for these groups were 23.6 (SD 8.6), 38.1 (SD 12.0), and 40.2 (SD 13.0), years, respectively. The corresponding figures for the duration of the reported asbestos exposures were 9.6 (SD 9.5), 12.1 (SD 14.7), and 13.1 (SD 15.7) years.

Discussion

The present results correspond well with results from previous studies[7–9] with regard to the prevalence rates of asbestos-related radiographic abnormalities in the general population. The results also confirm that the prevalence of pleural changes is higher in an urban than in a rural population. There was no clear relation to work-related exposures for the observed parenchymal changes. Along with the deviant age distribution in the two populations, the observed higher rate of such changes in the rural community could be related to other lung illnesses accompanied by fibrotic changes. Lung fibrosis is associated with tobacco smoking,[10] but pleural plaques are not. However, in light of the smoking habits in the two populations studied, it does not seem likely that the present findings can be explained by smoking.

Based on the primary screening with 10 × 10 cm films of 1388 men, 75 of them had previously been selected for a clinical reexamination, which included a 40 × 40 cm chest X-ray,[11] and an occupational history taken by interview.[2] At that examination 4 cases of pulmonary asbestosis, of which 3 also had pleural plaques, and 23 cases of pleural plaques only had been diagnosed. Table 3 presents the findings by the previous reexamination of large films in relation to findings by the

TABLE 3

Radiographic Findings by the ILO Classification of 10 × 10 cm Chest X-Rays and Questionnaire Information on Asbestos Exposure in Relation to Diagnosis Based on Findings on 40 × 40 cm Chest X-Rays and an Occupational History among 75 of the Study Subjects Who Had Previously Been Selected for a Clinical Reexamination

Findings by the ILO classification	Diagnosis at the clinical examination: Pulmonary asbestosis only $n = 1$	Pulmonary asbestosis ± pleural plaques $n = 3$	Pleural plaques only $n = 26$	Other pneumoconiosis $n = 4$*	No asbestos-related disease or other pneumoconiosis $n = 42$
Small opacities with profusion ≥ 1/0	0	1	1	2	3
Pleural changes	0	3	21	1	1
Confirmed asbestos exposure in questionnaire	0	3	13	1	18

* One person was regarded as having pulmonary asbestosis mixed with another pneumoconiosis.

present ILO classification of the 10 × 10 cm films from the same subjects. Among the 4 subjects with pulmonary asbestosis the ILO classification recognized only one with small opacities with profusion ≥ 1/0. Among 29 subjects with pleural plaques, the ILO classification recognized 24 (82.8%) with pleural changes (circumscribed or diffuse pleural thickening, or pleural calcification). However, when ILO findings were combined with questionnaire information on past asbestos exposure, the present ILO reevaluation classified only 16 subjects of the 30 (53.3%) as having an asbestos-related illness. Thus, the limiting factor of the present ILO reassessment in identifying asbestos-related illnesses, particularly pleural changes, in a population screening seems to be the low sensitivity of the questionnaire in detecting the exposed subjects.

The ILO 12-point scale of small opacities requires a comparison with standard films, which are available only in large sizes. This could be one reason why the sensitivity of the present reading to asbestos-related parenchymal changes was low. Such an explanation would be in keeping with the results presented by Sheers et al.,[12] who found that the agreement between small and large films was poorer for parenchymal changes than for pleural lesions. On the other hand, the same authors claimed that the reading method was more important than the size of the film with regard to the detection of asbestos-related changes. Weiss[10] found that small-size roentgenograms were as appropriate as large ones for both parenchymal and pleural changes. In the present study, the ILO classification of small films only proved to be more sensitive in detecting pleural changes than the previously conducted clinical two-stage reading of both small and large films. One obvious disadvantage of the ILO classification, however, is that it cannot firmly separate extrapleural fat from diffuse thickening of the pleura, or large plaques from diffuse thickening. This is particularly important for asbestos-related changes. Therefore, there has been a demand for a revision of the ILO system regarding pleural changes.[13]

Acknowledgments

The authors wish to thank the staff of the National Health Screening Service for their valuable contribution through all parts of the study.

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Erratum

Random keypunching errors were discovered after the publication of the article "Blood exposure and the risk of hepatitis B virus infection in firefighters."[1] Data from completed paper questionnaires were rekeypunched in duplicate and cross-checked. A reanalysis led to no substantial changes in results or conclusions; however, in the logistic regression analysis, one marginally significant odds ratio became nonsignificant. For this reason, a revised version of Table 5 from this article is included below.

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Reference

1. Woodruff BA, Moyer LA, O'Rourke KM, Margolis HS. Blood exposure and the risk of hepatitis B virus infection in firefighters. *J Occup Med.* 1993;35:1048–1054.

TABLE 5
Risk of HBV Infection in Fire Department Employees. Logistic Regression Analysis Including Factors Shown Important by Univariate Analysis

Risk factor	Category	Odds ratio	95% CI*
Race	Black	2.0	0.96, 4.3
	White	Referent	
History of STD	Yes	2.2	1.1, 4.4
	No	Referent	
Had blood contact with skin in prior 6 months	Yes	1.8	0.94, 3.6
	No	Referent	
Performed CPR without protective device in prior 6 months	Yes	1.8	0.7, 4.2
	No	Referent	

* Confidence interval.